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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|------------------------|------------------|
| 10/575,474 | 04/12/2006 | Hiroko Kojima | 062405 | 3422 |
| 38834 | 7590 | 04/09/2007 | EXAMINER | |
| WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP | | | SHEN, WU CHENG WINSTON | |
| 1250 CONNECTICUT AVENUE, NW | | | ART UNIT | PAPER NUMBER |
| SUITE 700 | | | 1632 | |
| WASHINGTON, DC 20036 | | | | |
| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | | DELIVERY MODE | |
| 3 MONTHS | 04/09/2007 | | PAPER | |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/575,474 | KOJIMA ET AL. | |
| | Examiner | Art Unit | |
| | Wu-Cheng Winston Shen | 1632 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-5 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

This application 10/575,474 filed on 04/12/2006 is a 371 of PCT/JP04/15673 filed on 10/15/2004 and claims the priority of foreign application JAPAN 2003-355505 filed on 10/15/2003.

Status of claims: claims 1-5 are currently under examination

Priority

1. This application 10/575,474 filed on 04/12/2006 is a 371 of PCT/JP04/15673 filed on 10/15/2004 and claims the priority of foreign application JAPAN 2003-355505 filed on 10/15/2003. The Examiner acknowledges that Applicant has submitted on 04/12/2006 a certified copy of PCT/JP04/15673 under requirement of 35 U.S.C. 119 (a-d) conditions. It is noted that no English translation of foreign application JAPAN 2003-355505 filed on 10/15/2003 has been provided and the foreign application JAPAN 2003-355505 was filed one year before the filing date of PCT/JP04/15673. Therefore, the priority of the claims of instant application is determined to be the PCT/JP04/15673 filed on 10/15/2004.

Claim Objections

2. Claims 1-5 are objected to because of the following informalities: claim 1 recites the phrase “a gene of an osteo-/chondro-inducible transcription factor”, which does not conform to the generally accepted scientific terms. It is noted that a gene refers to nucleic acid sequences

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that encodes a protein, which encompasses a transcription factor. Appropriate correction is required.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. (Yang et al., In vitro and in vivo synergistic interactions between the Runx2/Cbfal transcription factor and bone morphogenetic protein-2 in stimulating osteoblast differentiation. *J Bone Miner Res.* 18(4): 705-15, 2003).

Yang et al. teach bone regeneration requires interactions between a number of factors including bone morphogenetic proteins (BMPs), growth factors, and transcriptional regulators such as Runx2/Cbfal (Runx2). Yang et al. further teach that cells transduced with AdCMV-Runx2 (adenovirus-based expression vectors) strongly expressed osteoblast markers, such as alkaline phosphatase and osteocalcin, but formed only a weakly mineralized extracellular matrix

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in vitro. To measure *in vivo* osteogenic activity, virally transduced cells were subcutaneously implanted into immunodeficient mice (See abstract, Yang et al., 2003).

Thus, Yang et al. clearly anticipates claims 1-3 of instant invention.

4. Claims 1-5 are rejected under 35 U.S.C. 102(e) and under 35 U.S.C. 102(a) as being anticipated by Kumta et al. (Kumta et al., U.S Patent application Publication 2003/0219466, Publication date, Nov. 27, 2003, filed on Mar. 19, 2003).

Kumta et al. teach nanocrystalline hydroxyapatite particles and a method for production of the nanocrystalline hydroxyapatite particles. The nanocrystalline hydroxyapatite particles find use in tissue engineering applications, for example bone and tooth engineering and repair applications (See abstract, Kumta et al., 2003).

With regard to an implant consisting of an bioadaptable material and its association with DNA (claims 1 and 4 of instant application), Kumta et al. teach polymer matrices of use as a tissue engineering substrate as described typically are "bioerodible," or "biodegradable," unless a permanent matrix is desirable. The terms "bioerodible," or "biodegradable," as used refer to materials, which are enzymatically or chemically degraded *in vivo* into simpler chemical species. Either natural or synthetic polymers can be used to form the matrix, which can be implanted *in vivo* (See parag. [0118], column 12, Kumta et al., 2003). And the hydroxyapatite prepared by the methods described herein, for example complexed with a biomaterial such as DNA, may be associated with any suitable matrix (See parag. [0053], column 5, Kumta et al., 2003). Furthermore, Kumta et al. teach *adenoviral vector* mediated gene transfer (See parag.

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[0117], column 12; parag. [0044], column 4, Kumta et al., 2003), and expression of gene (See parag. [0042], column 4, Kumta et al., 2003).

With regard to Cbfal (claims 2 and 3 of instant application), Kumta et al. teach in one embodiment, the biomaterial is DNA that contains a gene, such as a bone morphogenetic protein gene. Examples of suitable genes include rhBMP-2 and *Runx2*. At the time of filing of instant application, *Runx2* is also known as Cbfal (core binding factor alpha 1) and Osf2 (osteoblast specific factor 2). For instance, Doll et al. (U.S. Patent Publication No: U.S. 2003/0235564, Publication date, Dec. 25. 2003) disclosed transcription factor *Runx2*, also referred to as Cbfal and as Osf2, which is a regulator of osteoblast differentiation (See parag. [0022], column 3, Doll et al. 2003).

With regard to β -TCP (β -tricalcium phosphate) (claims 4 and 5 of instant application), Kumta et al. teach the calcium deficient hydroxyapatite decompose into β -TCP and CaO accompanied by slight weight loss (See parag. [0086], column 9, Kumta et al., 2003).

Thus, Kumta et al. clearly anticipates claims 1-5 of instant invention.

5. Claims 1-5 are rejected under 35 U.S.C. 102(e) and under 35 U.S.C. 102(a) as being anticipated by Doll et al. (Doll et al., U.S Patent application Publication 2003/0235564, Publication date, Dec. 25, 2003, filed on May 13, 2003).

Doll et al. teach A pharmaceutical composition comprising in combination the *Runx2* protein, a polynucleotide encoding the *Runx2* protein, or a cell that has been transformed with a polynucleotide encoding *Runx2* protein, in a pharmaceutically acceptable carrier, the carrier

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comprising a bio-compatible, biodegradable polymeric matrix. Another aspect of the invention includes a device comprising the above-described pharmaceutical composition in combination with a sterile and substantially antigen-free, pre-shaped allograft or xenograft bone implant (See abstract, Doll et al., 2003).

With regard to an implant consisting of a bioadaptable material and its association with DNA (claims 1 and 4 of instant application), Doll et al. teach a method for repairing a bone defect comprising administering to a mammalian patient at the site in need of treatment a pharmaceutical composition, comprising in combination the Runx2 protein, a polynucleotide encoding the Runx2 protein, or a cell that has been transformed with *a polynucleotide encoding Runx2 protein*, in a pharmaceutically acceptable carrier wherein the carrier is a bio-compatible, biodegradable polymeric matrix (See abstract, Doll et al., 2003). Doll et al. teach viral vectors have higher transaction (ability to introduce genes) abilities than do most chemical or physical methods to introduce genes into cells. And the viral vectors include retroviral vectors and adenoviral vectors (See parag. [0096], [0097], and [0098], Doll et al., 2003).

With regard to Cbfal (claims 2 and 3 of instant application), Doll et al. teach transcription factor Runx2, also referred to as Cbfal (core binding factor alpha 1) and as Osf2 (osteoblast specific factor 2), which is a regulator of osteoblast differentiation (See parag. [0022], column 3, Doll et al. 2003).

With regard to β -TCP (β -tricalcium phosphate) (claims 4 and 5 of instant application), Doll et al. teach the reports on the use of β -tricalcium phosphate for implantation; and reports on the use of demineralized bone implants (See parag. [0053], column 7, Doll et al., 2003).

Thus, Kumta et al. clearly anticipates claims 1-5 of instant invention.

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Conclusion

6. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private

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Wu-Cheng Winston Shen, Ph. D.

Patent Examiner

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